RELATIONSHIP BETWEEN HIGH SENSITIVITY C-REACTIVE PROTEIN LEVEL AND ANGIOGRAPHIC SEVERITY OF THE DISEASE IN STEMI

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CERTIFICATE

This is to certify that the dissertation entitled "**RELATIONSHIP BETWEEN HIGH SENSITIVITY C-REACTIVE PROTEIN LEVEL AND ANGIOGRAPHIC SEVERITY OF THE DISEASE IN STEMI"**, is a bonafide record work done by **Dr. RAJESH KANNAN. S** under my direct supervision and guidance, submitted to the Tamil Nadu Dr.M.G.R Medical University regulation for **M.D Branch I – Medicine**.

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DECLARATION

I, **Dr. RAJESH KANNAN.S** solemnly declare that the dissertation titled **"RELATIONSHIP BETWEEN HIGH SENSITIVITY C-REACTIVE PROTEIN AND ANGIOGRAPHIC SEVERITY OF THE DISEASE IN STEMI"** has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of M.D degree **Branch – I (Medicine)** to be held in April 2012.

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CONTENTS

INTRODUCTION

Over the last decade, cardiovascular disease (CVD) has become the single largest cause of death worldwide.[1]They account for about 30% of all cause of death.[2] IHD is the most common, serious, chronic, life-threatening illness in the world.[2]

Traditional risk factors include modifiable and non-modifiable risk factors. Non modifiable risk factors include age, sex, race, family history, personal history. Modifiable risk factors include cigarette smoking, obesity, Physical inactivity, Kidney disease, Diabetes mellitus, Alcohol consumption, Stress, elevated LDL, and reduced HDL.[1, 3]

In recent years, new serum markers have been used in the diagnosis and risk stratification of patients with acute ischemic heart disease. These markers of myocardial damage are systematically employed in the diagnosis and prognosis of acute coronary syndromes.[4] It has been suggested that inflammation influences the pathogenesis of atherosclerosis and the progression of acute coronary syndromes.[5]

Consequently, markers of inflammation are also used in prognostic stratification of acute coronary syndromes.[6] Among these markers, C-reactive protein (CRP) is preferred because of its availability, stability, and prolonged average life.[7]

In this background a cross sectional study was done in 52 patients admitted with features of acute coronary syndrome. Hs-CRP was measured and level was compared to the angiographic severity of the lesion

REVIEW OF LITERATURE

Definition:

Patients with ischemic heart disease fall into two large groups:

Patients with chronic coronary artery disease (CAD) who most commonly present with stable angina and patients with acute coronary syndromes (ACSs). The latter group, in turn, is composed of patients with acute myocardial infarction (MI) with ST-segment elevation on their presenting electrocardiogram (ECG) (STEMI) and those with unstable angina (UA) and non-ST-segment elevation MI.

Acute Coronary Syndrome:

Revised Definition of Myocardial Infarction[8]

Criteria for Acute, Evolving, or Recent MI:

Either of the following criteria satisfies the diagnosis for acute, evolving, or recent MI:

1 Typical rise and/or fall of biochemical markers of myocardial necrosis with at least one of the following:

a. Ischemic symptoms

b. Development of pathologic Q waves in the ECG

c. E lectrocardiographic changes indicative of ischemia (ST-segment elevation or depression)

d. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality

2 Pathologic findings of an acute myocardial infarction

Criteria for Healing or Healed Myocardial Infarction:

Any one of the following criteria satisfies the diagnosis for healing or healed myocardial infarction:

1 D evelopment of new pathologic Q waves in serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarction developed.

2 Pathologic findings of a healed or healing infarction

Classification of Myocardial Infarction:

TYPE FEATURES

1 Spontaneous myocardial infarction related to ischemia caused by a primary coronary event s uch as plaque erosion and/or rupture, fissuring, or dissection

2. Myocardial infarction secondary to ischemia caused by increased

oxygen demand or decreased supply (e.g., coronary artery spasm, coronary embolism, anemia, arrhythmias, hypertension, hypotension)

3. Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischemia, accompanied by presumably new ST-segment elevation, or new L BBB, or presumably new major obstruction in a coronary artery by angiography and/or pathology, but death occurring before blood samples could be obtained, or before the appearance of cardiac biomarkers in the blood

4a Myocardial infarction associated with PCI

4b Myocardial infarction associated with stent thrombosis, as documented by angiography or autopsy

5 Myocardial infarction associated with CABG

Unstable angina and NSTEMI:

UA is defined as angina pectoris or equivalent ischemic discomfort with at least one of three features:

(1) It occurs at rest (or with minimal exertion), usually lasting >10 minutes;

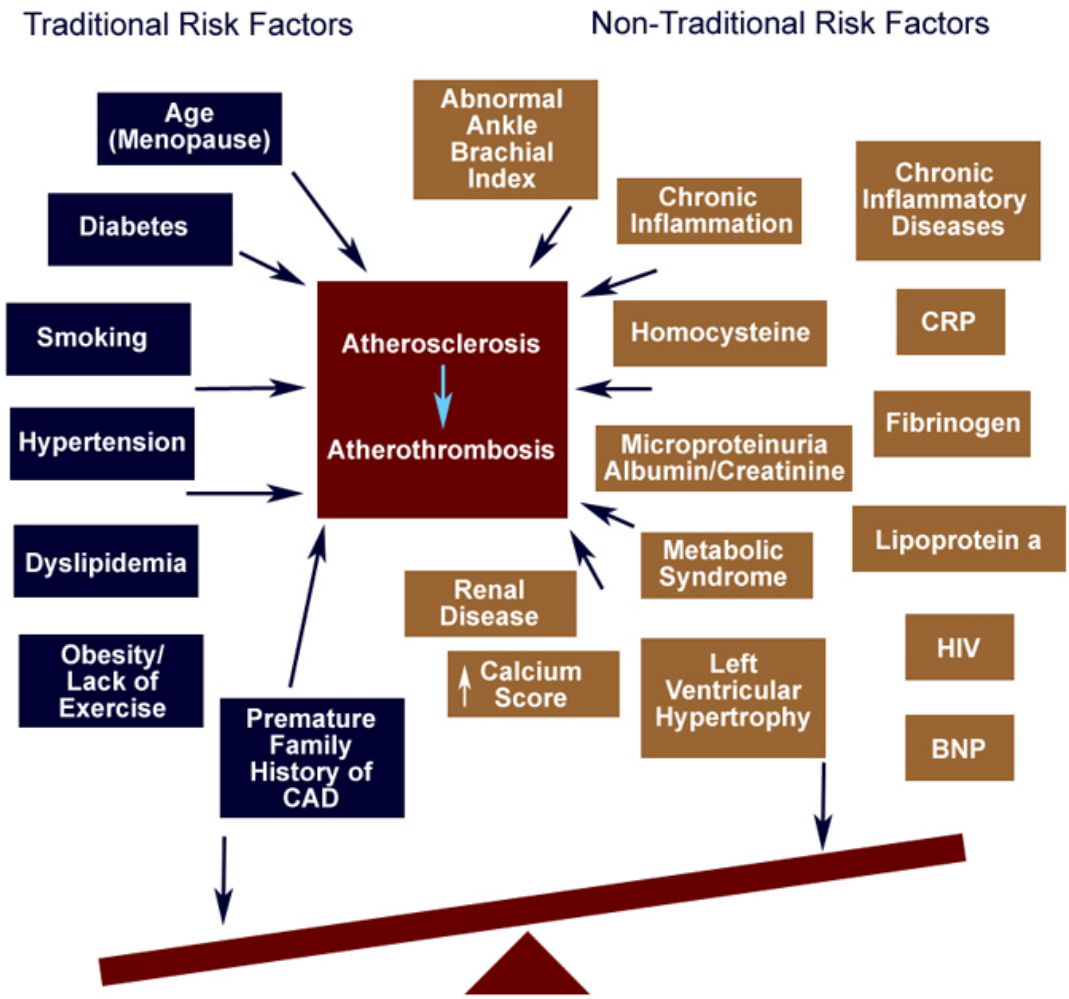
(2) It is severe and of new onset (i.e., within the prior 4–6 weeks); and/or

(3) It occurs with a crescendo pattern (i.e., distinctly more severe,

prolonged, or frequent than previously).

The diagnosis of NSTEMI is established if a patient with the clinical features of UA develops evidence of myocardial necrosis, as reflected in elevated cardiac biomarkers.[1, 2]

Risk factors:



Major Risk Factors for Coronary Artery Disease

-Age (men ≥ 45 years; women ≥ 55 years)
-Family history of premature coronary artery disease (CAD in male first-degree relative < 65 years)
-Hypertension (BP > 140/90 mmHg or on antihypertensive medications)
-Cigarette Smoking
-Diabetes
-Hypercholesterolemia
-Low HDL cholesterol (< 40 mg/dl)
-Hypertriglyceridemia (> 200 mg/dl)
-Obesity

Traditional risk factors:

Smoking:

Other than advanced age, smoking is the single most important risk factor for coronary artery disease. Cigarette consumption is the leading preventable cause of death in the United States, where it accounts for more than 400,000 deaths annually.[9] Ischemic heart disease causes 35% to 40% of all smoking-related deaths, with an additional 8% attributable to second-hand smoke exposure.

Cessation of cigarette consumption overwhelmingly remains the single most important intervention in preventive cardiology. In a major overview, smoking cessation was found to reduce CHD mortality by 36% as compared with mortality in subjects who continued smoking, an effect that did not vary by age, sex, or country of origin.[10]

Lipid disorders:

The Framingham Heart Study results demonstrated that the higher the cholesterol level, the greater the risk of coronary artery disease (CAD); alternatively, CAD was uncommon in people with cholesterol levels below 150 mg/dL. In 1984, the Lipid Research Clinics-Coronary Primary Prevention Trial revealed that lowering total and LDL or bad cholesterol levels significantly reduced CAD. More recent series of clinical trials using statin drugs have provided conclusive evidence that lowering LDL cholesterol reduces the rate of

myocardial infarction (MI), the need for percutaneous coronary intervention and the mortality associated with CAD-related causes.[11]

Hypertension:

Hypertension currently is defined as a usual BP of 140/90 mm Hg or higher, for which the benefits of drug treatment have been definitively established in randomized placebo-controlled trials.[12] High blood pressure often confers silent cardiovascular risk, and its prevalence is steadily increasing.

Hypertension, along with other factors such as obesity, have been said to contribute to the development of left ventricular hypertrophy (LVH). LVH has been found to be an independent risk factor to cardiovascular disease morbidity and mortality. It roughly doubles the risk of cardiovascular death in both men and women.[15]

Diabetes mellitus:

Insulin resistance and diabetes rank among the major cardiovascular risk factors; in one major survey, the presence of diabetes conferred an equivalent risk to aging 15 years, an impact higher than that of smoking.[13]

Obesity is associated with elevated vascular risk in population studies. In addition, this condition has been associated with glucose intolerance, insulin resistance, hypertension, physical inactivity, and dyslipidemia.[14]

Lack of activity:

The cardio protective benefits of exercise include reducing adipose tissue, which decreases obesity; lowering blood pressure, lipids, and vascular inflammation; improving endothelial dysfunction, improving insulin sensitivity, and improving endogenous fibrinolysis.[16]

Studies have also shown that even 15 minutes a day or 90 minutes a week of moderate-intensity exercise may be beneficial.[17]

Mental stress, depression, cardiovascular risk:

Depression has been strongly implicated in predicting CAD.[18]. Adrenergic stimulation during stress can increase myocardial oxygen requirements, can cause vasoconstriction, and has been linked to platelet and endothelial dysfunction[19] and metabolic syndrome.[20]

Non Traditional Risk Factors:

hs-CRP:

Inflammation characterizes all phases of atherothrombosis and provides a critical pathophysiologic link between plaque formation and acute rupture, which lead to occlusion and infarction.[21] The acute-phase reactant CRP, a simple downstream marker of inflammation, has now emerged as a major cardiovascular risk marker.[22]

Lipoprotein A:(LpA)

An elevated lipoprotein(a) [Lp(a)] level is an independent risk factor of premature CAD[23] and is particularly a significant risk factor for premature atherothrombosis and cardiovascular events. Measurement of Lp(a) is more useful for young individuals with a personal or family history of premature vascular disease and repeat coronary interventions.

Homocysteine:

Homocysteine is a sulfhydryl-containing amino acid derived from the demethylation of dietary methionine. Patients with rare inherited defects of methionine metabolism can develop severe hyperhomocysteinemia (plasma levels higher than 100 mmol/liter) and have a markedly elevated risk of premature atherothrombosis and venous thromboembolism.[1] In the general population, mild to moderate elevations are due to insufficient dietary intake of folic acid and folate antagonists.[1]

Other risk factors include ESRD, inflammatory markers like myeloperoxidase, IL-6, P-selectin, ICAM etc. are also potential risk factors for CAD.

Future Directions in Cardiovascular Risk Assessment:[1]

Some 40% of the U.S. adult population is at intermediate risk, but these individuals do not currently qualify for intensive risk factor intervention, despite the presence of one or more traditional risk factors. Current evidence suggests that the readiest tool to improve risk stratification among these individuals is the inflammatory biomarker hsCRP as an adjunct to global risk prediction. Strong evidence, as reviewed earlier, has shown that hsCRP adds prognostic information at all LDL-C levels of the Framingham risk score and of the metabolic syndrome. Thus, hsCRP evaluation, along with standard lipid screening and knowledge of family history, may become common practice in the near future. The pathophysiologic implications that follow from the inflammatory hypothesis of atherothrombosis should lead to novel interventions for primary prevention as well as for the treatment of acute ischemia.

Direct Plaque Imaging: [1]

In addition to the use of inflammatory markers and family history, strategies to detect vascular disease will likely take several forms. One approach eschews risk factor measurement, but identifies preclinical disease through the noninvasive detection of atherosclerotic plaque. Such an approach can never

truly prevent disease; it can only lead to early detection. However, because many therapies can delay clinical expression of disease once existing lesions are diagnosed, this approach merits consideration.

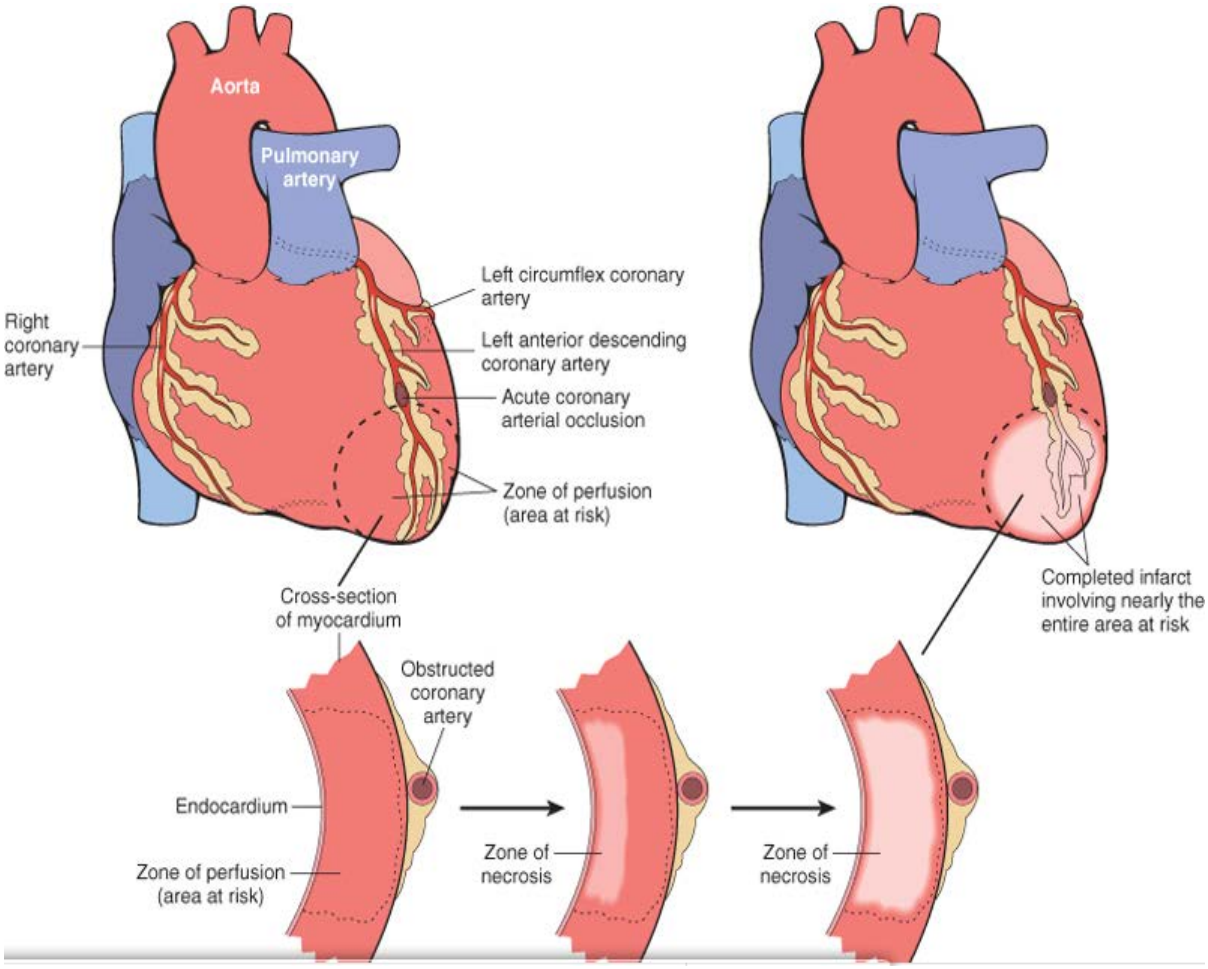
Several studies indicate that coronary calcification, as detected by computed tomography (CT), can detect preclinical atherosclerosis. Much controversy remains, however, as to whether this approach is cost-effective or has an acceptable false-negative rate. Enrollment in some of these studies may be biased by referral patterns or self-selection by patients. Part of the difficulty with coronary calcification as a clinical biomarker that CT imaging probably detects the plaques least likely to rupture and does not detect the less calcified lesions that appear to cause most clinical events. Thus, although coronary calcium provides a noninvasive measure of atherosclerotic burden, patients with low calcium scores cannot be dismissed as being at low risk. Furthermore, the clinical determinants of calcification are largely unknown and may not reflect propensity to plaque rupture. Studies indicating that hsCRP elevation corresponds to an approximate doubling of the risk of plaque rupture at all levels of coronary calcium have demonstrated the complexity of this approach. Although advocates of CT imaging have noted that sensitivity for the presence of angiographic coronary disease is comparable with that of noninvasive stress testing, such as perfusion scintigraphy or dobutamine echocardiography, the specificity of CT imaging in this setting is low.

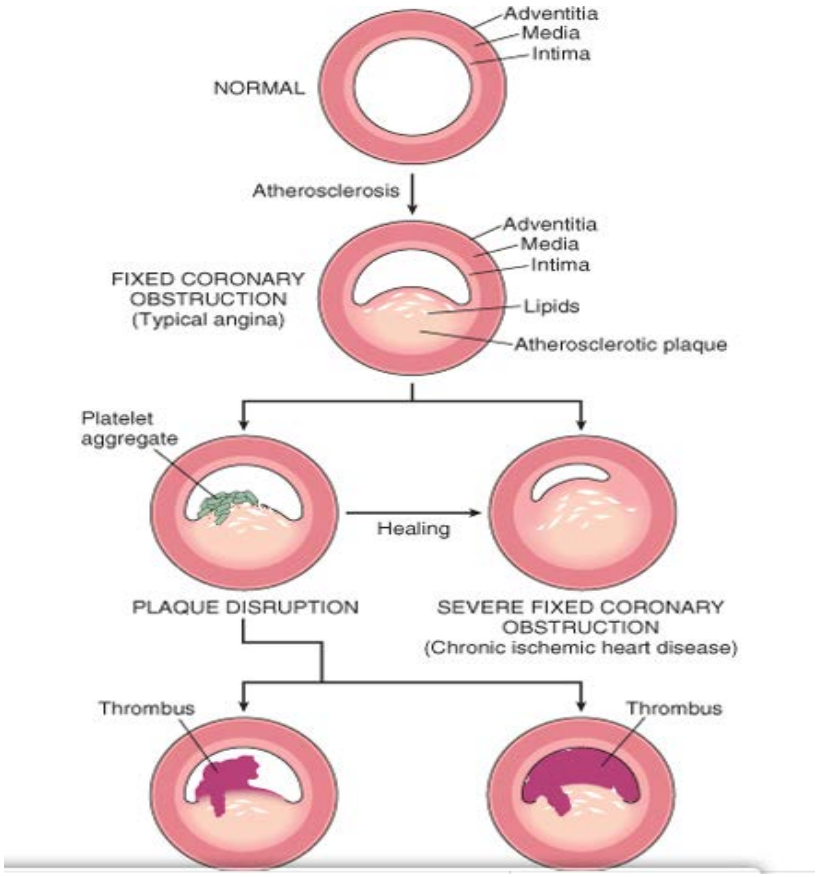
Pathophysiology of CAD/ACS:

Most commonly ACS results from ongoing atherosclerotic process but there are other causes for myocardial infarction like CTD, metabolic disorders, hematological, embolism, trauma, congenital anamolies.[1]

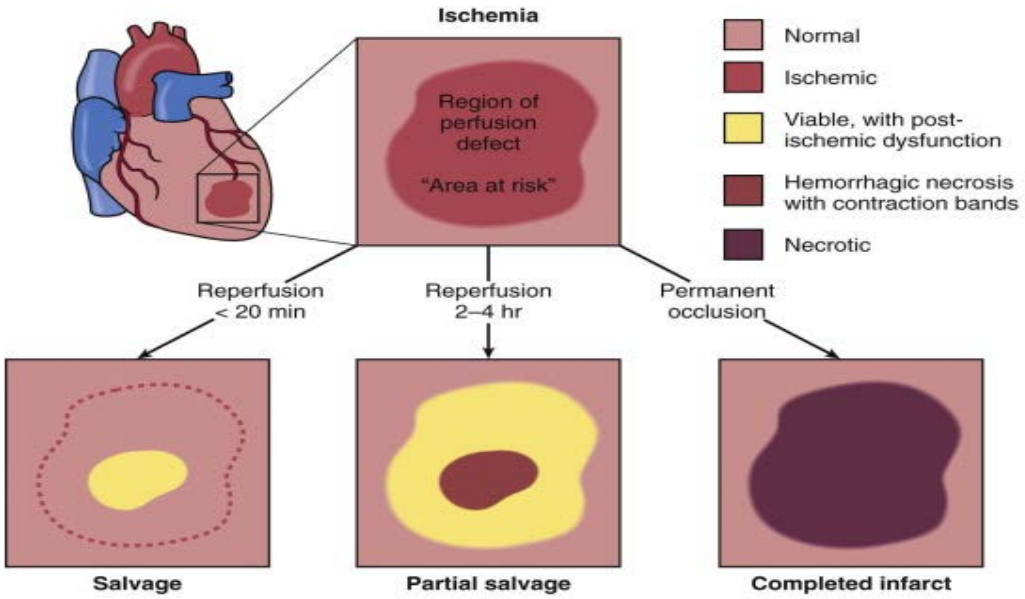
During the natural evolution of atherosclerotic plaques, especially lipid-laden plaques, an abrupt and catastrophic transition can occur, characterized by plaque disruption .[25,26] Some patients have a systemic predisposition to plaque disruption that is independent of traditional risk factors.[27] Plaque disruption exposes substances that promote platelet activation and aggregation, thrombin generation, and ultimately thrombus formation. The resultant thrombus interrupts blood flow and leads to an imbalance between oxygen supply and demand and, if this imbalance is severe and persistent, to myocardial necrosis.

By gross pathology MI can be divided as transmural and sub endocardial infarcts.[24] Ultra microscopy reveals various stages of repair and injury. [24] These changes can be potentially reversible when treated early.[1]


Aorta
Pulmonary artery
Left circumflex coronary artery
Right coronary artery
Left anterior descending coronary artery
Acute coronary arterial occlusion
Zone of perfusion (area at risk)
Completed infarct involving nearly the entire area at risk
Cross-section of myocardium
Obstructed coronary artery
Endocardium
Zone of perfusion (area at risk)
Zone of necrosis
Zone of necrosis


NORMAL
Adventitia
Media
Intima
Atherosclerosis
FIXED CORONARY OBSTRUCTION (Typical angina)
Adventitia
Media
Intima
Lipids
Atherosclerotic plaque
Platelet aggregate
Healing
PLAQUE DISRUPTION
SEVERE FIXED CORONARY OBSTRUCTION (Chronic ischemic heart disease)
Thrombus
Thrombus

1


Ischemia
Region of perfusion defect
"Area at risk"
Normal
Ischemic
Viable, with post-ischemic dysfunction
Hemorrhagic necrosis with contraction bands
Necrotic
Reperfusion < 20 min
Reperfusion 2–4 hr
Permanent occlusion
Salvage
Partial salvage
Completed infarct

Symptoms: [28]

1. Chest pain
2. Diaphoresis
3. Dyspnea
4. Fatigue
5. Light headedness
6. Palpitations
7. Acute confusion
8. Indigestion
9. Nausea vomiting

In up to one-half of cases, a precipitating factor appears to be present before STEMI, such as vigorous physical exercise, emotional stress, or a medical or surgical illness. Although STEMI may commence at any time of the day or night, circadian variations have been reported such that clusters are seen in the morning within a few hours of awakening.

Pain is the most common presenting complaint in patients with STEMI. The pain is deep and visceral; adjectives commonly used to describe it are heavy, squeezing, and crushing, although, occasionally, it is described as stabbing or burning. It is similar in character to the discomfort of angina pectoris but commonly occurs at rest, is usually more severe, and lasts longer.

Typically, the pain involves the central portion of the chest and/or the epigastrium, and, on occasion, it radiates to the arms. Less common sites of radiation include the abdomen, back, lower jaw, and neck. The frequent location of the pain beneath the xiphoid and epigastrium and the patients' denial that they may be suffering a heart attack are chiefly responsible for the common mistaken impression of indigestion. The pain of STEMI may radiate as high as the occipital area but not below the umbilicus. It is often accompanied by weakness, sweating, nausea, vomiting, anxiety, and a sense of impending doom. The pain may commence when the patient is at rest, but when it begins during a period of exertion, it does not usually subside with cessation of activity, in contrast to angina pectoris.

The pain of STEMI can simulate pain from acute pericarditis pulmonary embolism acute aortic dissection, costochondritis, and gastrointestinal disorders. These conditions should therefore be considered in the differential diagnosis. Radiation of discomfort to the trapezius is not seen in patients with STEMI and may be a useful distinguishing feature that suggests pericarditis is the correct diagnosis. However, pain is not uniformly present in patients with STEMI. The proportion of painless STEMIs is greater in patients with diabetes mellitus, and it increases with age. In the elderly, STEMI may present as sudden-onset breathlessness, which may progress to pulmonary edema. Other less common presentations, with or without pain, include sudden loss of consciousness, a

confusional state, a sensation of profound weakness, the appearance of an arrhythmia, evidence of peripheral embolism, or merely an unexplained drop in arterial pressure.

Signs:[29]

1. Signs of sympathetic activation: pallor, sweating, tachycardia

2. Signs of vagal activation: vomiting, bradycardia

3. Signs of impaired myocardial function

4. Hypotension, oliguria, cold peripheries

5. Narrow pulse pressure

6. Raised JVP

7. Third heart sound

8. Quiet first heart sound

9. Diffuse apical impulse

10. Lung crepitations

Signs of tissue damage : fever

Signs of complications : e.g. mitral regurgitation, pericarditis

Cardiac Examination:[1]

Palpation:

Palpation of the precordium may yield normal findings, but in patients with transmural STEMI, it m ore commonly reveals a presystolic pulsation, synchronous with an audible fourth heart sound, which reflects a vigorous left atrial contraction filling a ventricle with reduced compliance. In the presence of LV systolic dysfunction, an outward movement of the left ventricle can be palpated in early diastole, coincident with a third heart sound.

Auscultation:

Heart Sounds:

The heart sounds, particularly the first sound, are frequently muffled and occasionally inaudible immediately after the infarct, and their intensity increases during convalescence. A soft first heart sound may also reflect prolongation of the P-R interval. Patients with marked ventricular dysfunction and/or left bundle branch block may have paradoxical splitting of the second heart sound.

A fourth heart sound is almost universally present in patients in sinus rhythm with STEMI. However, it has limited diagnostic value because it is commonly audible in most patients with chronic ischemic heart disease and is recordable, although not often audible, in many normal subjects older than 45 years of age.

A third heart sound in patients with STEMI usually reflects severe LV dysfunction with elevated ventricular filling pressure. It is caused by rapid deceleration of transmitral blood flow during protodiastolic filling of the left ventricle and is usually heard in patients with large infarctions. This sound is detected best at the apex, with the patient in the left lateral recumbent position. A third heart sound may be caused not only by LV failure but also by increased inflow into the left ventricle, as occurs when mitral regurgitation or ventricular septal defect complicates STEMI. Third and fourth heart sounds emanating from the left ventricle are heard best at the apex; in patients with right ventricular infarcts, these sounds can be heard along the left sternal border and increase on inspiration.

Murmurs:

Transient or persistent systolic murmurs are commonly audible in patients with STEMI and generally result from mitral regurgitation secondary to dysfunction of the mitral valve apparatus (e.g., papillary muscle dysfunction, LV dilation). A new, prominent, apical holosystolic murmur, accompanied by a thrill, may represent rupture of a head of a papillary muscle . The findings in cases of rupture of the interventricular septum are similar, although the murmur and thrill are usually most prominent along the left sternal border and may be audible at the right sternal border as well. The systolic murmur of tricuspid regurgitation (caused by right ventricular failure because of pulmonary

hypertension and/or right ventricular infarction or by infarction of a right ventricular papillary muscle) is also heard along the left sternal border. It is characteristically intensified by inspiration and is accompanied by a prominent *c-v* wave in the jugular venous pulse and a right ventricular fourth sound.

Friction Rubs:

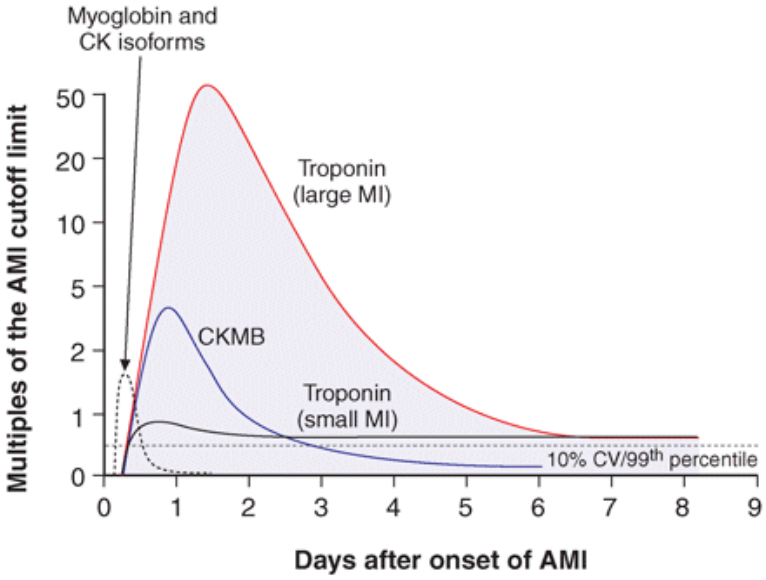
Pericardial friction rubs may be heard in patients with STEMI, especially those sustaining large transmural infarctions. Rubs are notorious for their evanescence and hence are probably even more common than reported. Although friction rubs can be heard within 24 hours or as late as 2 weeks after the onset of infarction, most commonly they are noted on the second or third day. Occasionally, in patients with extensive infarction, a loud rub can be heard for many days. Patients with STEMI and a pericardial friction rub may have a pericardial effusion on echocardiographic study, but only rarely does this cause the classic electrocardiographic changes of pericarditis. Delayed onset of the rub and the associated discomfort of pericarditis (as late as 3 months postinfarction) are characteristic of the now rare postmyocardial infarction syndrome (Dressler syndrome).

Pericardial rubs are most readily audible along the left sternal border or just inside the apical impulse. Loud rubs may be audible over the entire precordium and even over the back. Occasionally, only the systolic portion of a rub is heard; it can be confused with a systolic murmur, and the diagnosis of

rupture of the ventricular septum or mitral regurgitation may be incorrectly considered

Investigations:

Cardiac enzymes:



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These considerations apply directly to patients on the UA/NSTEMI end of the ACS spectrum, a general discussion of cardiac biomarkers is presented here because the scientific aspects of the pathophysiologic concepts and assay methodology overlap when biomarkers are used to evaluate STEMI patients. It should be emphasized that clinicians should not wait for the results of biomarker assays to initiate treatment for the STEMI patient. Because there is time urgency for reperfusion in STEMI, the 12-lead ECG should serve to initiate such strategies.[1]

Necrosis compromises the integrity of the sarcolemmal membrane; intracellular macromolecules (serum cardiac markers) begin to diffuse into the cardiac interstitium, and ultimately into the microvasculature and lymphatics in the region of the infarct .The rate of appearance of these macromolecules in the peripheral circulation depends on several factors, including intracellular location, molecular weight, local blood and lymphatic flow, and rate of elimination from the blood.[1]

Echocardiograpy:

The relative portability of echocardiographic equipment makes this technique ideal for the assessment of patients with MI hospitalized in the coronary care unit or even in the emergency department before admission .[86] In patients with chest pain compatible with MI but with a

Non-diagnostic ECG, the finding of a distinct region of disordered contraction on echocardiography can be helpful diagnostically because it supports the diagnosis of myocardial ischemia. Echocardiography can also help evaluate patients with chest pain and a nondiagnostic ECG who are suspected of having an aortic dissection. The identification of an intimal flap consistent with an aortic dissection is a cr itical observation because it represents a m ajor contraindication to fibrinolytic therapy.[1]

Other investigations include CT, Cardiac MRI, nuclear imaging. The estimate of the infarct size can be done by ECG, enzymes and Cardiac MRI.

CRP and hs-CRP:

CRP, named for its capacity to precipitate the somatic C-polysaccharide of Streptococcus pneumoniae, was the first acute-phase protein to be described and is an exquisitely sensitive systemic marker of inflammation and tissue damage . The acute-phase response comprises the nonspecific physiological and biochemical responses of endothermic animals to most forms of tissue damage, infection, inflammation, and malignant neoplasia. In particular, the synthesis of a number of proteins is rapidly upregulated, principally in hepatocytes, under the control of cytokines originating at the site of pathology. Other acute-phase proteins include proteinase inhibitors and coagulation, complement, and transport proteins, but the only molecule that displays sensitivity, response speed, and dynamic range comparable to those of CRP is serum amyloid A protein (SAA).

In healthy young adult volunteer blood donors, the median concentration of CRP is 0.8 mg/l, the 90^{th} centile is 3.0 mg/l, and the 99th centile is 10 mg/l , but, following an acute-phase stimulus, values may increase from less than 50 µg/l to more than 500 mg/l, that is, 10,000-fold. Plasma CRP is produced only by hepatocytes, predominantly under transcriptional control by the cytokine IL-6, although other sites of local CRP synthesis and possibly secretion have been suggested. De novo hepatic synthesis starts very rapidly after a single stimulus, serum concentrations rising above 5 mg/l by about 6

hours and peaking around 48 hours. The plasma half-life of CRP is about 19 hours and is constant under all conditions of health and disease, so that the sole determinant of circulating CRP concentration is the synthesis rate , which thus directly reflects the intensity of the pathological process(es) stimulating CRP production. When the stimulus for increased production completely ceases, the circulating CRP concentration falls rapidly, at response, such as plasma viscosity and the erythrocyte sedimentation rate. Importantly, acute-phase CRP values show no diurnal variation and are unaffected by eating. Liver failure impairs CRP production, but no other intercurrent pathologies and very few drugs reduce CRP values unless they also affect the underlying pathology providing the acute-phase stimulus. The CRP concentration is thus a very useful nonspecific biochemical marker of inflammation, measurement of which contributes importantly to (a) screening for organic disease, (b) monitoring of the response to treatment of inflammation and infection, and (c) detection of intercurrent infection in immunocompromised individuals, and in the few specific diseases characterized by modest or absent acute-phase responses . It is not known why systemic lupus erythematosus and the other conditions listed with it in table fail to elicit major CRP production despite evident inflammation and tissue damage, nor why the CRP responses to intercurrent infection are apparently intact in patients with such conditions

CRP in Disease process:[31]

1.Infection:

1. Bacterial Systemic infection
2. Severe fungal infections
3. Mycobacterial infections
4. Viral infection

2.Allergic complications:

1. Rheumatic fever

3.Inflamatory

1. Erythema nodosum
2. Rheumatoid arthritis
3. Juvenile chronic arthritis
4. Ankylosing spondylitis
5. Psoriatic arthritis,
6. Systemic vasculitis
7. Polymyalgia rheumatica
8. Reiter disease
9. Crohn disease
10. Familial Mediterranean fever

4. Necrosis

1. Myocardial infarction
2. Tumor embolization
3. Acute pancreatitis

5. Trauma

1. Surgery
2. Burns
3. Fractures

6.Malignancy

1. Lymphoma
2. Carcinoma
3. Sarcoma

Functions of CRP:

i. It recognizes and 'scavenges' cellular debris and promotes its clearance.

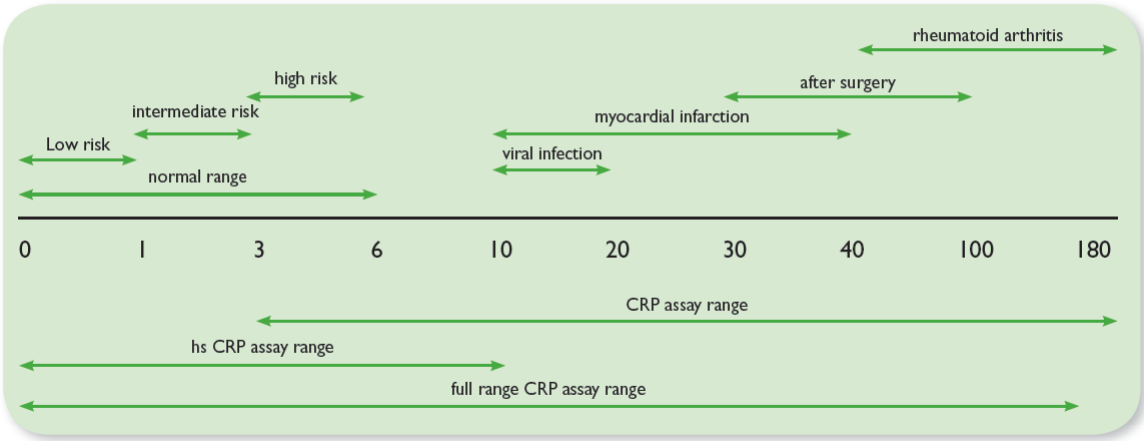
ii. Protects against infection with pneumococci and H. Influenza. iii. Complement activation by CRP exacerbates ischaemic injury.

iv. It is proatherogenic – by binding to phospholipids and lipoproteins.

v. It is prothrombotic – CRP stimulates tissue factor production by macrophages.

vi. CRP suppresses polymorph migration (which is anti-inflammatory).

CRP levels showing cardiac risk and diseases



hs-CRP levels could be used for risk assessment and as a diagnostic and prognostic marker in myocardial infarction patients .[32]

Treatment:

Risk stratification:[28]

1 Age

2. Systolic blood pressure

3. Killip classification

4. Heart rate

5. Location of MI

These five parameters account for 90% of the prognostic information for 30 day mortality.

Antithrombotic Agents:[2]

The use of antiplatelet and anticoagulant therapy during the initial phase of STEMI is based on extensive laboratory and clinical evidence that thrombosis plays an important role in the pathogenesis of this condition. The primary goal of treatment with antiplatelet and anticoagulant agents is to maintain patency of the infarct-related artery, in conjunction with reperfusion strategies. A secondary goal is to reduce the patient's tendency to thrombosis and, thus, the likelihood of mural thrombus formation or deep venous thrombosis, either of which could result in pulmonary embolization. The degree to which antiplatelet and anticoagulant therapy achieves these goals partly determines how effectively it reduces the risk of mortality from STEMI.

Aspirin is the standard antiplatelet agent for patients with STEMI. The most compelling evidence for the benefits of antiplatelet therapy (mainly with aspirin) in STEMI is found in the comprehensive overview by the Antiplatelet Trialists' Collaboration. Data from nearly 20,000 patients with MI enrolled in 15 randomized trials were pooled and revealed a relative reduction of 27% in the mortality rate, from 14.2% in control patients to 10.4% in patients receiving antiplatelet agents.

Inhibitors of the P2Y12 ADP receptor prevent activation and aggregation of platelets. The addition of the P2Y12 inhibitor clopidogrel to background treatment with aspirin to STEMI patients reduces the risk of clinical events (death, reinfarction, stroke) and, in patients receiving fibrinolytic therapy, has been shown to prevent reocclusion of a successfully reperfused infarct artery. New P2Y12 ADP receptor antagonists, such as prasugrel and ticagrelor, are more effective than clopidogrel in preventing ischemic complications in STEMI patients undergoing PCI, but are associated with an increased risk of bleeding. Glycoprotein IIb/IIIa receptor inhibitors appear useful for preventing thrombotic complications in patients with STEMI undergoing PCI.

The standard anticoagulant agent used in clinical practice is unfractionated heparin (UFH). The available data suggest that when UFH is added to a regimen of aspirin and a non-fibrin-specific thrombolytic agent such as streptokinase, additional mortality benefit occurs (about 5 lives saved per 1000 patients treated). It appears that the immediate administration of intravenous UFH, in addition to a regimen of aspirin and relatively fibrin-specific fibrinolytic agents (tPA, rPA, or TNK), helps to maintain patency of the infarct-related artery. This effect is achieved at the cost of a small increased risk of bleeding. The recommended dose of UFH is an initial bolus of 60 U/kg (maximum 4000 U) followed by an initial infusion of 12 U/kg per hour

(maximum 1000 U /h). The activated partial thromboplastin time during maintenance therapy should be 1.5–2 times the control value.

Alternatives to UFH for anticoagulation of patients with STEMI are the low-molecular-weight heparin (LMWH) preparations, a synthetic version of the critical pentasaccharide sequence (fondaparinux), and the direct antithrombin bivalirudin. Advantages of LMWHs include high bioavailability permitting administration subcutaneously, reliable anticoagulation without monitoring, and greater antiXa:IIa activity. Enoxaparin has been shown to reduce significantly the composite endpoints of death/nonfatal reinfarction and death/nonfatal reinfarction/urgent revascularization compared with UFH in STEMI patients who receive fibrinolysis. Treatment with enoxaparin is associated with higher rates of serious bleeding, but net clinical benefit—a composite endpoint that combines efficacy and safety—still favors enoxaparin over UFH. Interpretation of the data on fondaparinux is difficult because of the complex nature of the pivotal clinical trial evaluating it in STEMI. Fondaparinux appears superior to placebo in STEMI patients not receiving reperfusion therapy, but its relative efficacy and safety compared with UFH is less certain. Owing to the risk of catheter thrombosis, fondaparinux should not be used alone at the time of coronary angiography and PCI but should be combined with another anticoagulant with antithrombin activity such as UFH or bivalirudin. Contemporary trials of bivalirudin used an open-label design to evaluate its

efficacy and safety compared with UFH plus a glycoprotein IIb/IIIa inhibitor. Bivalirudin was associated with a l ower rate of bleeding. Patients with an anterior location of the infarction, severe LV dysfunction, heart failure, a history of embolism, two-dimensional echocardiographic evidence of mural thrombus, or atrial fibrillation are at increased risk of systemic or pulmonary thromboembolism. Such individuals should receive full therapeutic levels of anticoagulant therapy (LMWH or UFH) while hospitalized, followed by at least three months of warfarin therapy.

Emergency CABG:

May be the treatment of in whom the intent is to perform direct or rescue percutaneous mechanical reperfusion but are found to have a critical left main stem lesion or severe triple vessel disease unapproachable with percutaneous revascularization. Right ventricular myocardial infarction is a relative contraindication to bypass surgery.

AIMS AND OBJECTIVES

1. To study the level of Hs-CRP in patient with acute coronary syndrome.
2. To study relationship between the level of Hs-CRP and disease severity graded by angiography.

MATERIAL AND METHODS

Setting : This work was done at Government Rajaji Hospital, affiliated to the Madurai Medical College, Madurai.

Collaborating Department : Department of Medicine in collaboration with departments of Cardiology and biochemistry

Design of study : Cross sectional and analytical study.

Period of study : April 2011 to October 2011.

Ethical approval : Approval for the study was obtained from the ethical committee of Government Rajaji Hospital, Madurai.

Consent : Prior informed consent was obtained from all the cases included in the study.

Sample size : 52 patients admitted with cardiology with diagnosis of acute coronary syndrome (STEMI)

Selection of study subjects:

Cases: First ever myocardial infarction patients admitted to Govt. Rajaji Hospital, who satisfied the inclusion criteria were selected for the study.

Inclusion criteria:

i. ECG changes suggestive of Acute Myocardial Infarction

ii. Echocardiography – presence of regional wall motion abnormalities

iii. Elevated enzymes – CPK

Exclusion criteria:

i. Chronic Kidney Disease

ii. Extra cardiac Atherosclerosis

iii. Acute / chronic liver diseases

iv. Rheumatoid arthritis

v. Documented connective tissue disorders

vi. Previous h/o Myocardial Infarction / CAD

vii. Fever within 1 week prior to admission

viii. Skin infections / any other overt infections

ix. Malignancy

x. Children

xi. Pregnant women

Socio demographic data

Age

Sex

Socio demographic and clinical data were collected. The study subjects were subjected to relevant investigations.

Clinical details:

Systolic and diastolic blood pressures were measured.

General and Systemic examination was done.

Cardiovascular risk factors were assessed.

Laboratory data:

- Blood urea estimation was done manually by using diacetyl monoxime (DAM) method.
- Serum creatinine estimation was done by using COBAS auto analyser
- Lipid profile, CPK, sugar estimation was done
- Serum Hs CRP estimation was done by immune turbidometry method
- ECG 12 lead Electro Cardio Gram was done
- ECHO – Echo Cardio Graphic evaluation was done
- ANGIO was done as a part of the work up and treatment of the patient.

Definitions used for this study:

Acute myocardial infarction: As defined by new consensus

Limitations of this study:

1. Many comorbid conditions influence on the hs CRP level

2. Serial estimation of hs CRP was not done in this study.

Financial support : Nil

Conflicting interest : Nil

Statistical analysis:

Data was prepared in Microsoft excel spread sheet. Analysis of data was done utilizing the software - Epidemiological Information Package 2010(Epi info 2010) developed by the Centers for Disease Control and Prevention-Atlanta, USA for World Health Organization and open EPI 2.3.1. Mean standard deviation and 'p' values were calculated using this package. Chi Square test and ANOVA was done where ever necessary to find out significance of relationship between the groups. Pearson's correlation was done to find the correlation of the values.

TABLES AND INTERPRETATION

In the present study 52 cases of First ever myocardial infarction (AMI) satisfied rigid selection criteria. Their age ranged from 23 years to 67 years and the mean ± S.D. was 48.6 ± 10.3 years. They were divided into three groups on the basis of the CRP levels.

Table 1: Age distribution between the study groups

AGE (yrs)	**GROUP 1** n=22	**GROUP 2** n=14	**GROUP 3** n=12
25-35	2	1	0
36-45	9	2	2
46-55	10	4	6
56-65	4	5	3
66-75	1	2	1
Range	29 – 67	30 – 73	40 – 67
Mean	48.61	56.42	53.41
SD	9.91	12.02	8.69

P=0.07 not significant

The patient groups did not differ statistically with reference to age.

Chart 3: Age distribution in the study groups.

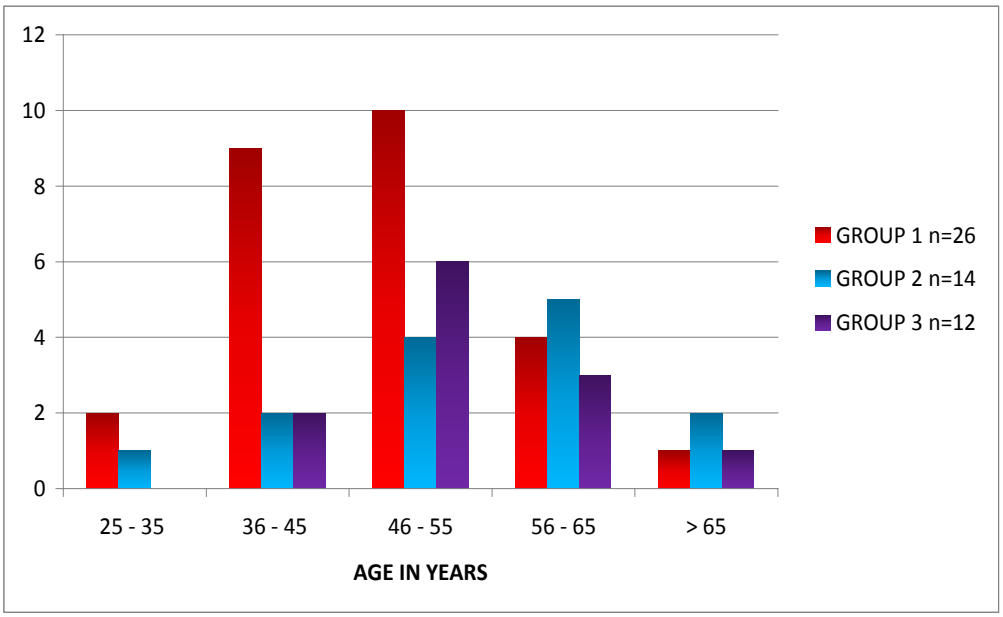
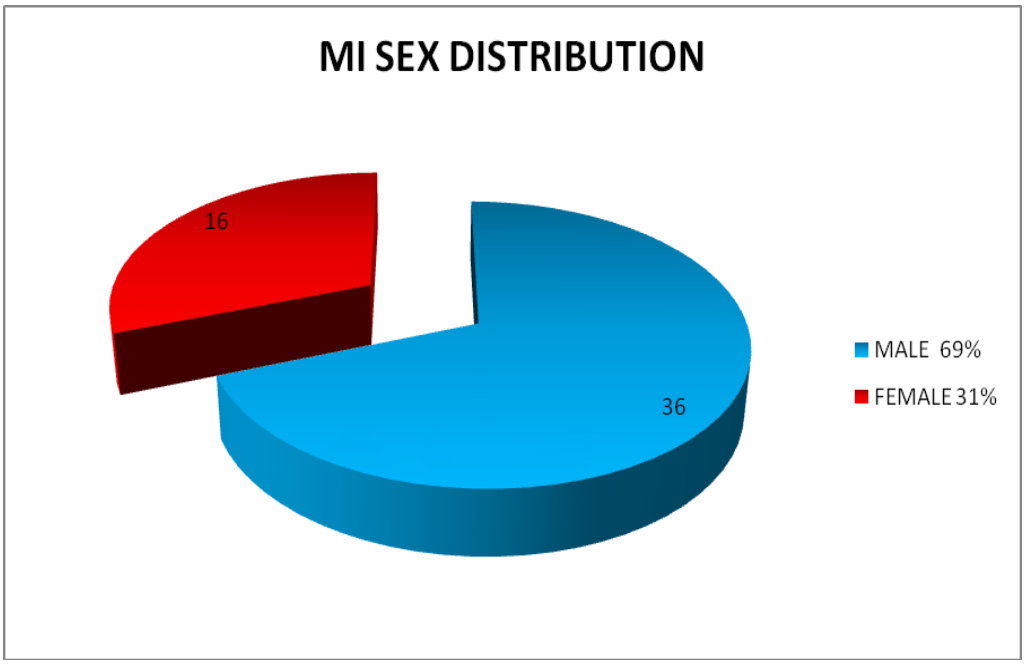


Chart 4: Incidence of MI according to sex.



Among the 52 cases 36 were male and 16 were female. The distribution within each group is as follows in the table

Table 2: Sex distribution between the groups

SEX	**GROUP 1** n=22	**GROUP 2** n=14	**GROUP 3** n=12
MALE	19	7	10
FEMALE	7	7	2

P=0.154 not significant

The patients groups did not differ statistically with reference to sex distribution.

Chart 1: Sex distribution in the study group.

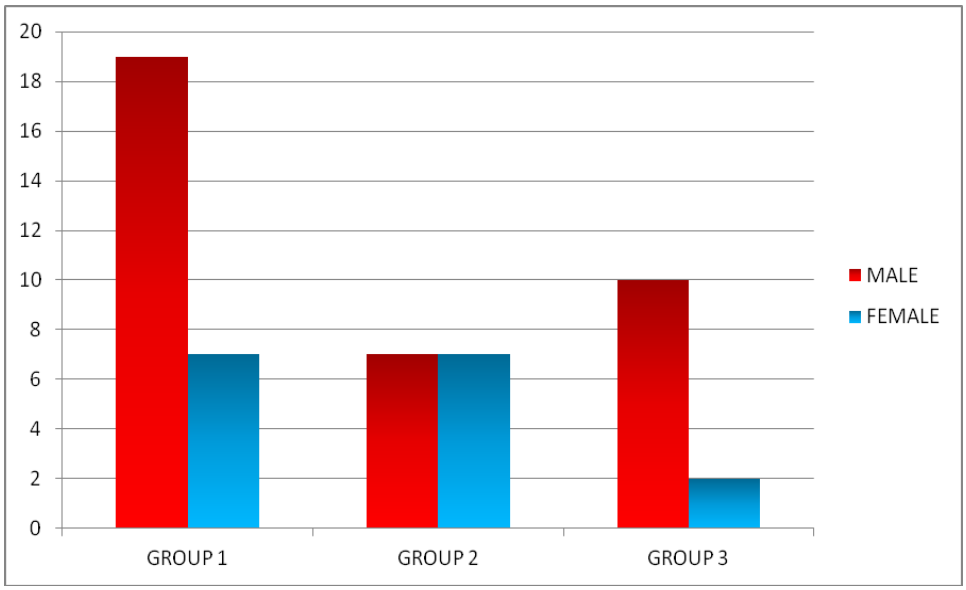
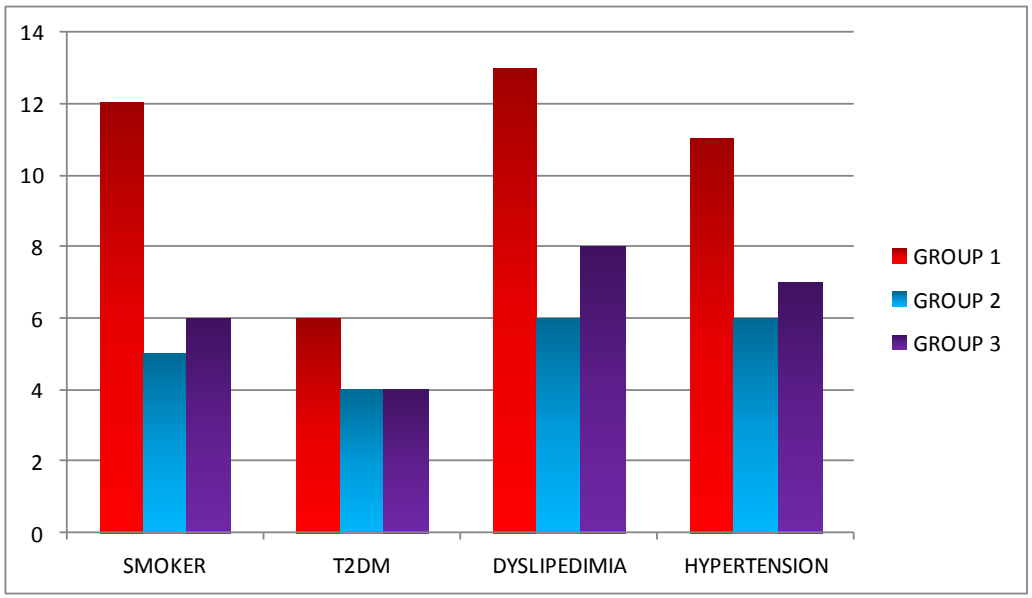


Chart 2: Risk factor distribution in the study groups.



Risk Factors distribution in the study group.

They following are the risk factor distribution in the three sub groups

Table 3:

SMOKER	GROUP 1 n=26	GROUP 2 n=14	GROUP 3 n=12	P VALUE
YES	12 46.14%	5 35.71%	6 50%	0.736*
NO	14 53.86%	9 64.29%	6 50%	

Table 4:

HTN	GROUP 1 n=26	GROUP 2 n=14	GROUP 3 n=12	P VALUE
YES	11 42.30%	6 42.85%	7 58.39%	0.627*
NO	15 57.7%	8 57.15%	5 41.61%	

Table 5:

T2DM	GROUP 1 n=26	GROUP 2 n=14	GROUP 3 n=12	P VALUE
YES	6 23.07%	4 28.57%	4 33.33%	0.792*
NO	20 76.93%	10 71.43%	8 66.67%	

Table: 6

DYSLIPIDEMIA	GROUP 1 n=26	GROUP 2 n=14	GROUP 3 n=12	P VALUE
YES	13 50%	6 42.85%	8 66.67%	0.462*
NO	13 50%	8 57.15%	4 33.33%	

***= not significant**

The patients groups did not differ statistically with reference to the risk factors.

BMI

Table 7:

BMI	GROUP 1 n=26	GROUP 2 n=14	GROUP 3 n=12
RANGE	20.81 – 29.00	21.67 – 29.96	20.02 – 27.513
MEAN	25.32	26.45	25.49
SD	2.32	2.43	1.91

p= 0.583 not statistically significant

Thus BMI is independent of CRP levels.

Chart 5: Relationship between vessel score and CRP level.

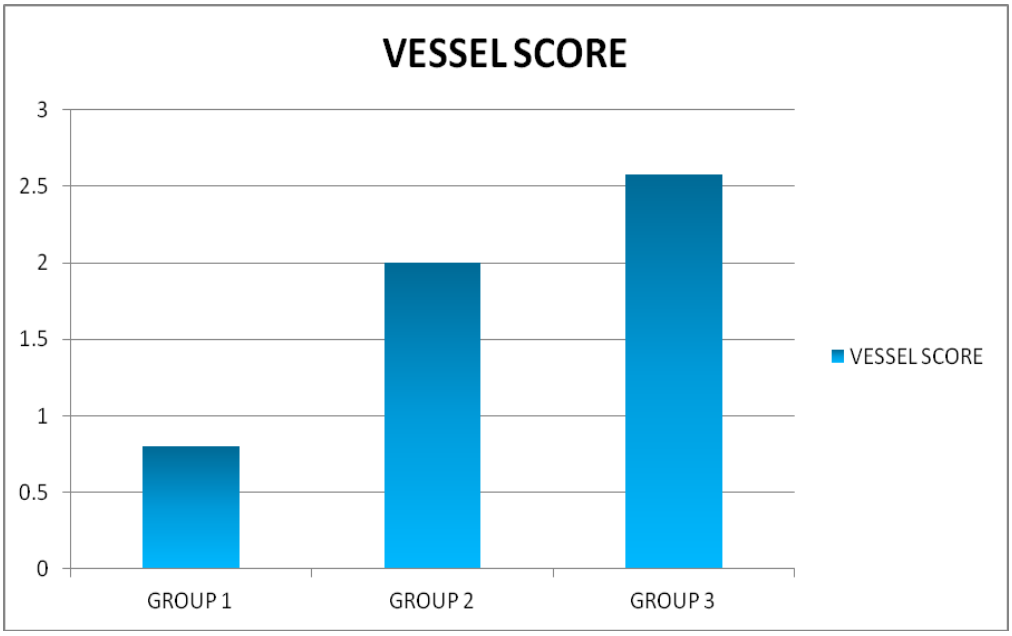


Chart 6: Scatter diagram of vessel score and CRP level.

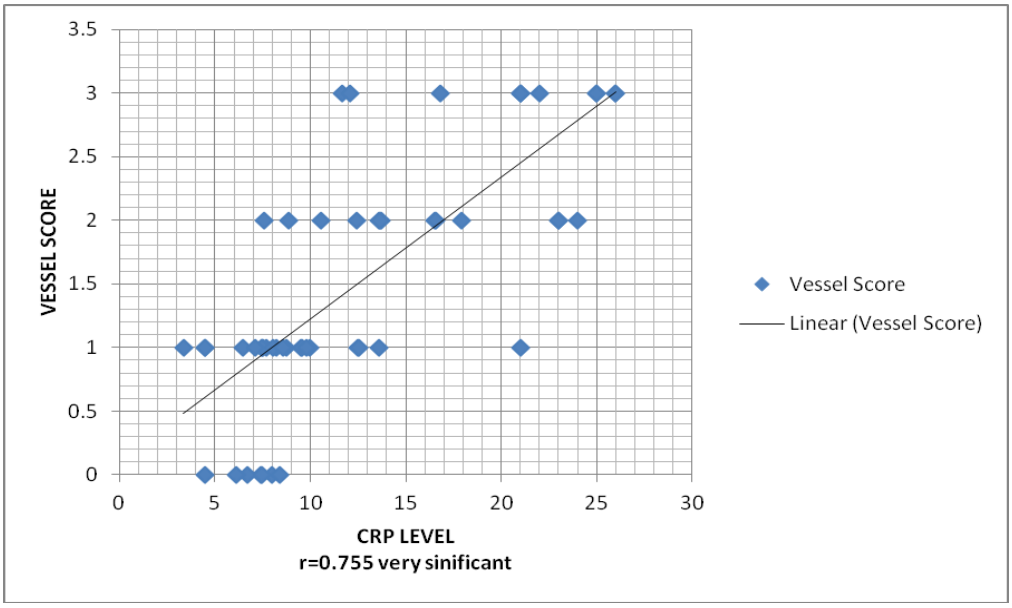


Table 8:

Relationship between HS CRP level and Vessel Score

	VESSEL SCORE				
	Range	Mean	S.D	'p' value	Significance
Group 1	0 – 2	0.8	0.55	<0.001	Significant
Group 2	0 – 3	2	0.65		
Group 3	0 – 3	2.58	0.64		

P Value < 0.001

The vessel score significantly correlates with the level of CRP.

Spearman correlation coefficient is r=0.755 which is statistically significant.

Chart 7: Relationship between stenosis score and CRP level.

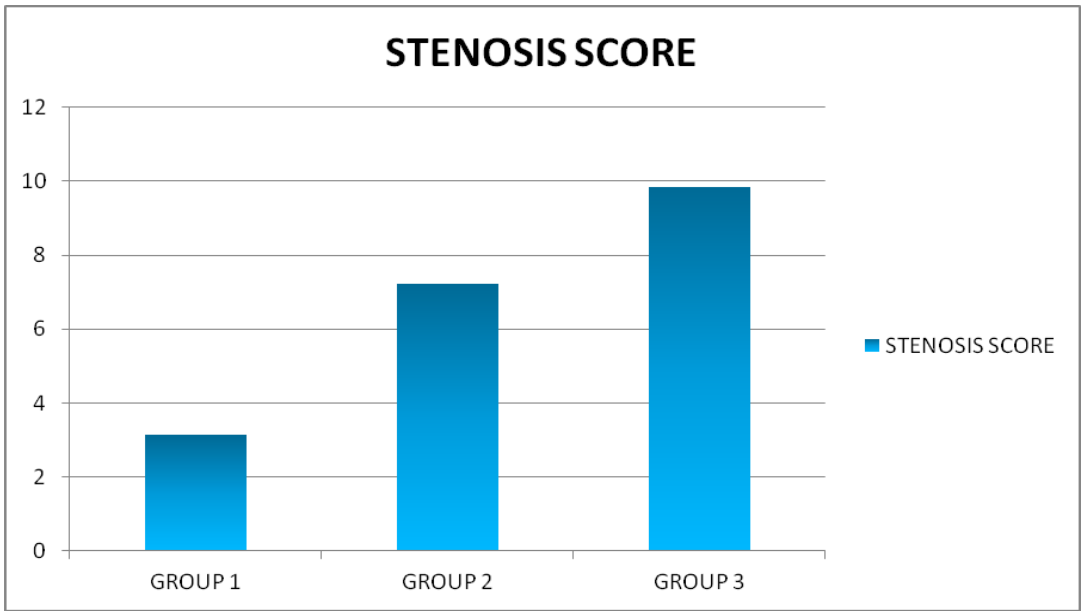


Chart 8: Scatter diagram of stenosis score and CRP level.

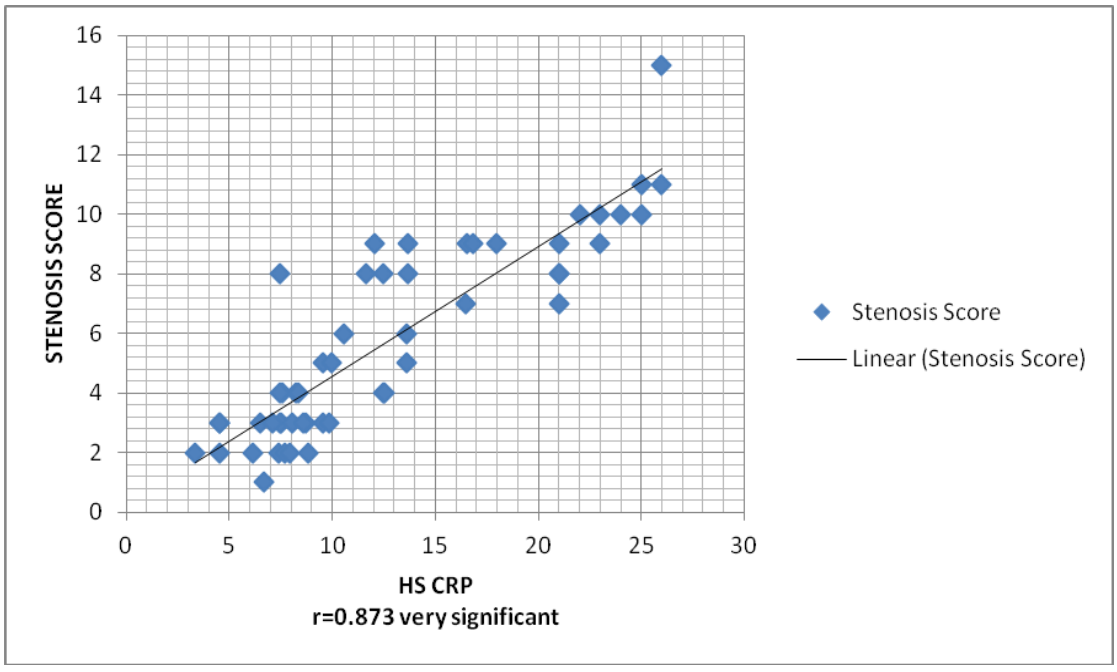


Table 9:

Relationship between HS CRP level and Stenosis Score

	STENOSIS SCORE				
	Range	Mean	S.D	'p' value	Significance
Group 1	0 – 5	3.15	1.34	< 0.001	Significant
Group 2	0 – 9	7.21	1.81		
Group 3	0 – 15	9.83	0.95		

P Value < 0.001

Spearman correlation coefficient is r=0.873 which is statistically significant.

The stenosis score significantly correlates with the level of CRP.

Chart 9: Relationship between extent score and CRP level.

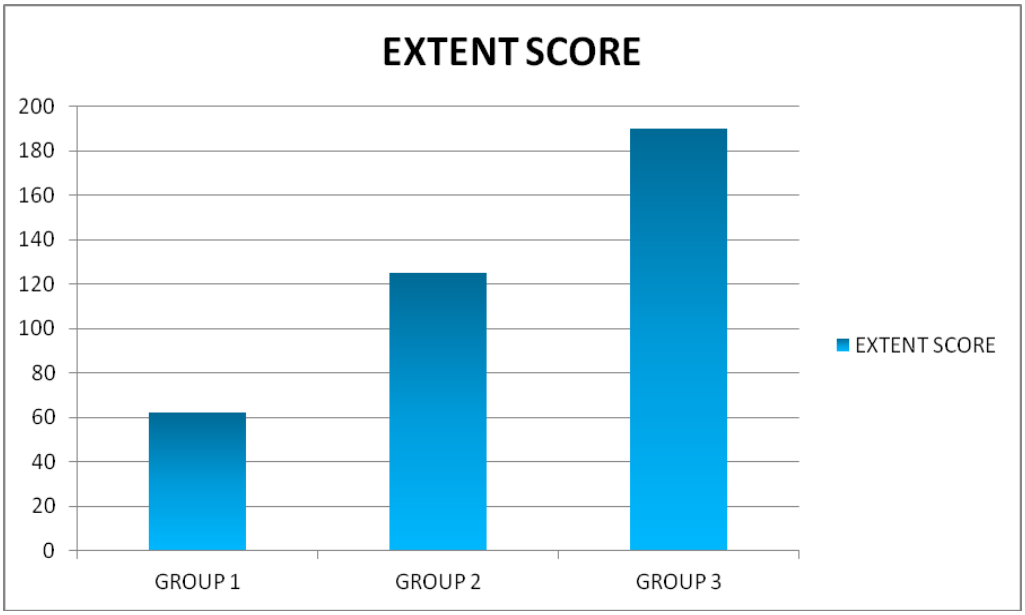


Chart 10: Scatter diagram of extent score and CRP level.

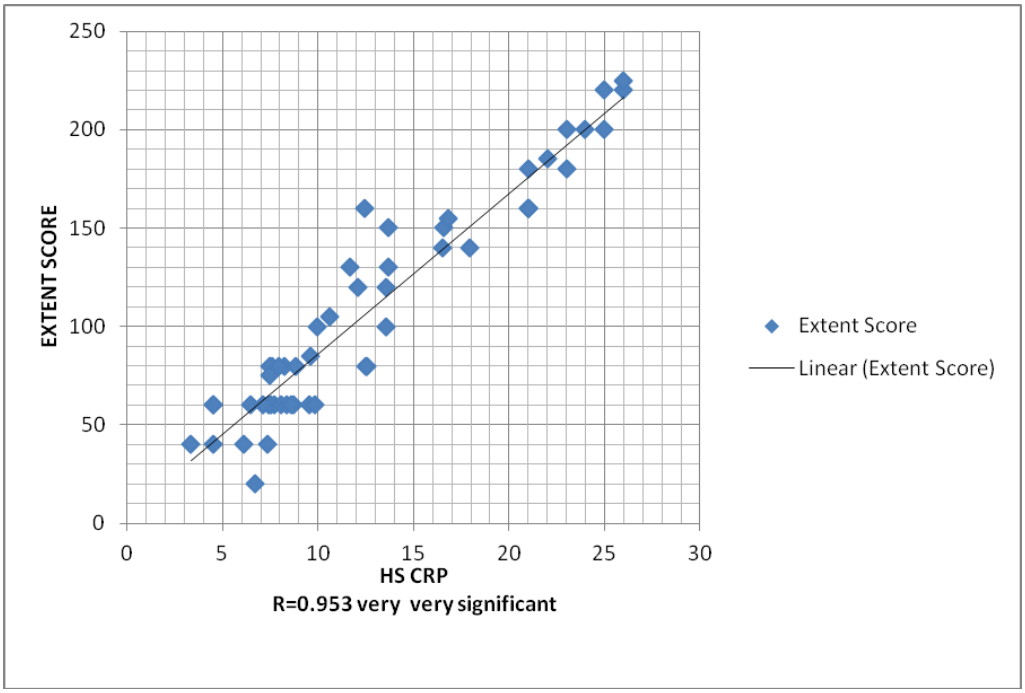


Table 10:

Relationship between HS CRP level and Extent Score

	EXTENT SCORE				
	Range	Mean	S.D	'p' value	Significance
Group 1	0 – 100	62.30	7.52	< 0.001	Significant
Group 2	0 – 150	125.71	25		
Group 3	0 – 225	190.83	22.80		

P Value < 0.001

Spearman correlation coefficient is r=0.953 which is statistically significant.

The extent score significantly correlates with the level of CRP.

DISCUSSION

CRP as novel risk factor in coronary artery disease:

A number of large, prospective epidemiologic studies have indicated that hs-CRP is a strong independent predictor of future cardiovascular events, including myocardial infarction, ischemic stroke, peripheral vascular disease, and sudden cardiac death among individuals without known CVD.[40,41]

The association between elevated hs-CRP levels and future CHD events has generally been consistent among these studies: subjects in the top quartile of hs-CRP levels have a 2 to 3 times greater relative risk of a future coronary event than do those in the bottom quartile.[42]

The strongest correlation between hs-CRP and risk of myocardial infarction occurred in those men without other risk factors – Honolulu heart program.[43]

The risk of cardiovascular disease burden increases with total cholesterol level.[44] Thus hs-CRP adds to the values of the lipid profile. The AHA/CDC guidelines support the use of hs-CRP in primary prevention and set cutoff points according to relative risk categories: low risk (1.0 mg/L), average risk (1.0–3.0 mg/L), and high risk (>3.0 mg/L).[45]

CRP in Acute coronary Syndrome:

C-reactive protein (CRP) is the classical acute phase reactant, the serum level of which has long been known to increase after myocardial infarction.[46, 47] All patients with definite myocardial infarction mounted a CRP response and there was a statistically significant correlation between the peak levels of CRP and of CK MB.[49] There was steady increase in the CRP level which gradually fell down after a week. Persistently elevated CRP level was associated with increased morbidity and mortality.[49]

CRP value ≥15 mg/L identify patients with HF at entry, it also predicted worsening of LV function in patients without clinical signs of HF at entry. Conversely, low first-day CRP values in patients with acute myocardial infarction at entry predicted improvement of Killip class in the subsequent days. Furthermore, in agreement with the results by others, peak CRP value was a strong independent predictor of all-cause and HF mortality during the following year. Although the precise role of CRP requires further elucidation, a focus on CRP within the first 3 days after acute myocardial infarction may prove useful for identification of patients who are at greater risk of heart failure and mortality.[49]

CRP and angiographic severity of the lesion:

Several studies prove that a high value of CRP correlates with severity and complexity of the lesion. Both angiographic complexity of the culprit lesion and elevated troponin level are related with increased C-reactive protein levels in non-ST elevation acute coronary syndromes in a study by Sanchís J, et al[50]

CRP levels predict future cardiovascular events independently of CAD severity and correlate with number of angiographically complex coronary artery stenosis in patients with ACS. Thus, CRP levels are a marker of atheromatous plaque vulnerability and CAD activity according to R. Arroyo-Espliguero et al.[51]

The level of C-reactive protein (CRP) can be used to identify patients with the most complicated coronary lesions and the greatest degree of intracoronary thrombosis, but it can also help identify patients with apparently non-complex lesions that are susceptible to rupture - a problem that would lead to patient instability.[52]

There is clear trend that hs-CRP level correlates significantly with angiographic features of thrombi and eccentric lesions.[53]

Significantly higher hs-CRP levels are found in angiographically proven CAD patients with acute coronary syndrome as compared to patients with normal coronary angiography; and the levels of hs-CRP correlated well with the angiographic severity of the CAD in study by Tenzin Nyandak et al.[54]

Angiographic grading of the lesions:

The modified Gensini score is one of the scoring systems for the grading of the severity of the coronary vasculature and extent of the disease.

Recently SYNTAX score has been used to grade the complexity of the lesion. This score is actually intended to plan patient for PTCA or CABG according to the score. A score of 1 – 22 means PTCA is favorable. A score greater than 33 favors CABG. Higher scores were associated with increased mortality and morbidity.

The Gensini scoring system is utilized in the evaluation of CAD severity. The Gensini score was calculated for each patient from the coronary arteriogram by assigning a severity score to each coronary stenosis according to the degree of luminal narrowing and its geographic importance. Reduction in the lumen diameter, and the roentgenographic appearance of concentric lesions and eccentric plaques were evaluated.

The stenosis score has a total score of 32 and the extent score calculated from the product of stenosis score and the segment score. The total extent score is 400. The vessel score ranges from 0 -3 according to the number of vessel involved.

In our study the mean age group was 48.6 with a deviation of this was similar to age group distribution as Masood et al[33]. In the study by Peppes et al[34] the age distribution was 60 with a deviation of 10.9 years.

There was no significant association between the three sub groups for age distribution.

The risk factor were not significantly associated with the CRP levels as reported by Tenzin Nyandak et al[54] and Masood et al.[33]

Danesh et al.[35] reported that in general, CRP concentrations increase among smokers with increased cigarette consumption. Regarding the smoking status it was found in this current study that 46.14%, 35.71% and 50% was smoker in group I, group II and group III respectively. This was inferior to the study by hansat et al.[37]

Koenig et al[36] have shown in their series 50.0 percent of the patients were hypertensive which is a l ittle inferior to the present study, where the current study observed that hypertensive was 42.30% in group I, 42.85% in group II and 58.33% in group III.

In the present study, diabetes mellitus was observed in 23.07% in group I, 28.57% in group II, 33.33% in group III. It is lower when compared to the study by Hansat et al.[37]

The CRP levels were consistently elevated in patients with myocardial infarction. Peppes et al[34] and H. Honarmand et al[39] reported the similar findings. The CRP levels well correlated with the vessel score, stenosis score and the extent score. This was similar to the reports by Peppes et al[34] , Arslan Masood et al[38] Hansat et al[37] and Tenzin Nyandak et al.[54]

CONCLUSION

1. Sex ratio of male to female in this study is 7:3
2. Highest incidence of myocardial infarction is in the age group of 46 – 55 years
3. Women had higher incidence of myocardial infarction in the postmenopausal age
4. CRP level is found consistently elevated in the patients developing myocardial infarction
5. Significant positive correlation was observed between the extent of coronary artery disease and hs-CRP levels. Similarly hs-CRP levels were found to be higher in patients with higher degree of angiographic stenosis. This shows that hs-CRP levels have a positive correlation with the disease burden in CAD patients.

Thus hs-CRP level may help in predicting the outcome of the patient admitted with acute myocardial infarction.

ABBREVIATIONS

ACS	–	Acute Coronary Syndrome
STEMI	–	ST Elevation Myocardial Infarction
NSTEMI	–	Non ST Elevation Myocardial Infarction
CAD	–	Coronary Artery Disease
CRP	–	C Reactive protein
hs CRP	–	High Sensitivity C Reactive Protein
CT	–	Computed Tomography
LVH	–	Left Ventricular Hypertrophy
ECHO	–	Echocardiography
ECG	–	Electrocardiogram
MI	–	Myocardial Infarction
Lp A	–	Lipoprotein A
CPK	–	Creatine Phosphokinase
HDL	–	High Density Lipoprotein
LDL	–	Low Density Lipoprotein
VLDL	–	Very Low Density Lipoprotein
TGL	–	Triglycerides
MRI	–	Magnetic Resonance Imaging

PROFORMA

NAME:			IP NO:
AGE/SEX:	HT:	WT:	BMI:

PRESENTING COMPLAINTS:

PERSONEL H/O & MEDICAL H/O:

SMOKER:	DIABETIC:
ALCOHOLIC:	HYPERTENSIVE:
DIET:	CRF:
POST MENOPAUSAL:	PREVIOUS H/O MI:

TREATMENT H/O:

ECG:

DIAGNOSIS:

TREATMENT GIVEN:

ECHO:

BLOOD INVESTIGATIONS:

UREA	
SUGAR	
CREATININE	
CPK TOTAL	
CPK MB	
hs CRP	
TC	
DC P L M E B	

LIPID PROFILE	
CHL	
HDL	
LDL	
TGL	
VLDL	

ANGIO REPORT:

NOTES:

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MASTER CHART

S.No.	NAME	AGE	SEX	HT	WT	BMI	SMOKER	T2DM	HTN	DYSLIPEDIMIA	POSTMENO PAUSAL	HSCRP	UREA	SUGAR	CREATININE	CPK TOT	TC	ECHO	EF	VESSEL SCORE	STENOSIS SCORE	EXTENT SCORE
1	SADASIVAM	59	M	1.65	55	20.20	Y	Y	Y	Y	_	23	26	263	1.3	338	11200	IWMI	45	2	9	180
2	MUTHU PANDI	45	M	1.64	78	29.00	Y	N	Y	Y	_	4.5	20	140	0.8	400	10000	AWMI	48	0	2	40
3	CHINNAIAH	65	M	1.48	60	27.39	Y	N	Y	N	_	21	32	90	12	434	7000	IWMI	45	3	7	160
4	VELLAMMAL	45	F	1.68	67	23.74	N	Y	N	Y	Y	8.72	32	341	0.8	231	8900	IWMI	40	1	3	60
5	SUNDARAM	47	M	1.59	64	25.32	N	N	Y	N	_	7.57	19	119	1.2	350	10300	IWMI	49	2	4	80
6	MARTEEN	42	M	1.72	70	23.66	Y	Y	Y	N	_	12.48	19	336	0.9	200	7200	IWMI	47	1	4	80
7	SHANMUGANATHAN	52	M	1.55	79	32.88	N	Y	Y	N	_	8.24	28	232	0.8	577	9700	AWMI	44	1	4	80
8	OYYANDI	60	M	1.58	58	23.23	Y	N	N	Y	_	7.37	23	60	0.9	600	13600	IWMI	50	0	2	40
9	MEENAL	60	F	1.66	75	27.22	N	N	Y	Y	Y	16.5	23	63	0.9	268	12500	IWMI	60	2	7	140
10	MURUGAN	42	M	1.7	76	26.30	Y	N	Y	Y	_	6.48	29	63	1	558	7500	AWMI	54	1	3	60
11	MANI	54	M	1.65	69	25.34	Y	Y	N	N	_	7.68	28	69	0.8	536	13800	AWMI	40	1	2	60
12	JEYALAKSMI	46	F	1.55	50	20.81	N	N	Y	N	N	9.52	20	87	0.9	533	6500	IWMI	45	1	3	60
13	PAULSAMY	55	M	1.63	63	23.71	N	N	N	N	_	12.45	26	86	1	364	10600	AWMI	35	2	8	160
14	KANNAN	31	M	1.68	70	24.80	Y	Y	N	N	_	7.45	21	62	1	298	6000	AWMI	40	1	4	80
15	CHINNAPONNU	55	F	1.54	55	23.19	N	N	Y	Y	Y	8.85	20	107	0.6	354	8400	AWMI	42	2	2	80
16	PALANIAMMAL	39	F	1.56	52	21.37	N	N	N	N	N	4.5	18	60	0.7	144	10000	IWMI	58	1	3	60
17	RAMA RAO	65	M	1.68	70	24.80	Y	Y	Y	Y	_	7.96	31	109	1.1	238	9300	AWMI	32	0	2	80
18	POOVALINGAM	37	M	1.66	75	27.22	Y	N	N	N	_	9.57	16	139	1	191	12300	AWMI	36	1	5	85
19	SONAI	50	M	1.7	78	26.99	Y	Y	Y	Y	_	26	41	360	1.3	247	14200	IWMI	45	3	11	220
20	NATARAJAN	40	M	1.61	70	27.01	Y	N	Y	Y	_	7.5	32	128	1.2	659	12800	AWMI	40	1	3	60
21	PITCHAI	40	M	1.59	59	23.34	N	N	N	N	_	7.43	18	108	0.7	167	13800	AWMI	33	1	3	60
22	MAHALINGAM	29	M	1.69	72	25.21	Y	N	N	Y	_	6.69	17	131	0.8	99	14500	AWMI	40	0	1	20
23	MARUDHAN	54	M	1.72	75	25.35	Y	N	Y	N	_	13.69	24	65	0.6	93	7700	IWMI	55	2	8	130
24	JEGATAMBAL	62	F	1.67	70	25.10	N	N	N	Y	N	11.64	22	137	0.7	548	11600	IWMI	58	3	8	130
25	KARANAN	40	M	1.71	74	25.31	Y	N	Y	Y	_	24	42	387	0.8	566	17000	IWMI	60	2	10	200

26	MURUGAN	48	M	1.65	59	21.67	N	N	Y	Y	_	22	19	150	0.8	300	19600	AWMI	33	3	10	185
27	MUTHAMMAL	70	F	1.64	65	24.17	N	N	N	Y	Y	12.07	47	76	1.2	766	8700	IWMI	36	3	9	120
28	PANDIARAJAN	50	M	1.56	60	24.65	N	N	N	N	_	21	44	126	0.7	1168	7800	AWMI	42	3	8	160
29	KRISHNAN	67	M	1.55	65	27.06	N	Y	Y	Y	_	25	55	235	1.2	300	12300	IWMI	42	3	10	200
30	SYEDHAMMAL	58	F	1.55	60	24.97	N	Y	Y	N	Y	13.58	19	85	1.1	197	10900	AWMI	36	1	5	100
31	PARVATHY	53	F	1.53	55	23.50	N	N	N	N	N	26	46	280	0.9	484	7300	AWMI	40	3	15	225
32	ALAGAN	52	M	1.66	67	24.31	N	N	N	Y	_	25	45	125	0.8	459	15000	IWMI	52	3	11	220
33	ALGARSAMY	55	M	1.72	74	25.01	Y	N	Y	N	_	3.35	36	169	1.1	390	8900	AWMI	48	1	2	40
34	MEHBOOB BEGAM	63	F	1.55	72	29.97	N	N	N	N	Y	16.56	42	106	1	590	13000	IWMI	46	2	9	150
35	SUSEELA	65	F	1.58	65	26.04	N	N	N	N	Y	23	19	121	0.9	350	15600	AWMI	56	2	10	200
36	VASANTHA	55	F	1.62	66	25.15	N	N	Y	N	Y	4.5	32	113	0.7	480	7500	IWMI	54	1	3	60
37	SATHYAMOORTHY	73	M	1.65	69	25.34	Y	N	N	Y	_	16.83	23	142	1.1	418	12400	IWMI	48	3	9	155
38	RENGARJ	45	M	1.68	60	21.26	Y	N	N	N	_	21	40	155	0.7	700	13000	IWMI	58	3	9	180
39	POOCHIAMMAL	60	F	1.59	65	25.71	N	N	N	Y	Y	8.05	15	140	0.8	653	9500	AWMI	49	1	3	60
40	MOORTHY	30	M	1.63	70	26.35	Y	Y	N	N	_	12.54	22	89	0.8	590	6000	AWMI	52	1	4	80
41	MUTHULAKSMI	65	F	1.69	73	25.56	N	N	N	N	Y	17.94	38	105	1.1	500	11000	IWMI	45	2	9	140
42	THANGAVEL	60	M	1.7	73	25.26	Y	N	N	Y	_	7.48	41	151	1.2	457	7800	IWMI	57	0	8	75
43	SANKARAN	67	M	1.73	74	24.73	N	N	N	Y	_	9.95	18	300	1	760	11300	AWMI	54	1	5	100
44	THEVAR	53	M	1.66	70	25.40	N	Y	Y	N	_	8.37	26	211	0	500	11000	AWMI	50	0	4	60
45	RAVI	37	M	1.65	59	21.67	Y	N	N	Y	_	10.58	29	149	0.9	190	12400	IWMI	55	2	6	105
46	AYYANAR	40	M	1.78	79	24.93	N	N	N	Y	_	8.58	35	98	0.6	298	11500	AWMI	50	1	3	60
47	BABUJI	55	M	1.61	70	27.01	N	N	Y	Y	_	13.59	22	79	0.7	495	15000	AWMI	54	2	6	120
48	DEIVANAI	54	F	1.52	62	26.84	N	Y	N	N	Y	13.67	19	166	0.9	570	13000	AWMI	41	2	9	150
49	ERRAMMAL	55	F	1.53	63	26.91	N	N	N	Y	Y	7.1	31	237	1.1	360	9000	AWMI	59	1	3	60
50	KARUPPAIAH	45	M	1.65	69	25.34	Y	N	N	N	_	6.13	34	100	1.2	300	7800	AWMI	57	0	2	40
51	SELVA KUMAR	47	M	1.64	74	27.51	Y	Y	Y	Y	_	21	16	63	0.6	560	17000	IWMI	48	1	8	160
52	SELVAN	47	M	1.56	68	27.94	N	N	N	Y	_	9.82	37	92	1.1	213	14300	IWMI	48	1	3	60